

# SILICON MICROMACHINED HOLLOW MICRONEEDLES FOR TRANSDERMAL LIQUID TRANSFER

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## ABSTRACT

This paper presents an improved design and fabrication process [1] for hollow micro needles with the proper mechanical strength and sharpness to be applied for painless transdermal transfer of liquids. Tests have shown that liquids like blood are drawn into the needle by capillary forces, reducing the need for active pumping. The fabrication method allows different needle shapes like blades and pencils, is robust enough to be applied for larger-scale production, and enables the development of a complete micro-TAS for e.g. blood analysis.

## INTRODUCTION

Nowadays, typical routes for drug delivery are either through hypodermic needles or by oral administration, while diagnostic sampling in most cases requires extraction of blood through a hypodermic syringe needle, followed by analysis of blood components in a specialized laboratory environment. During the last decades, it has become clear that the introduction of MEMS offers exciting opportunities to advance the medical field, the buzzword being "minimally invasive". The latter is associated with limited tissue damage and pain reduction. In addition, miniaturization of analysis methods enables the development of versatile portable equipment for "Point-of-care" monitoring and treatment of patients. This trend will eventually lead to Internet-based healthcare monitoring systems that allow medical specialists to track the patient's situation on-line, or that give patients the choice to be more directly involved in monitoring their own health, thereby increasing the chances of improving their quality of life and reducing healthcare expenses. Ultimately, the advancement in the field may reach the state of drug-on-demand possibilities, by which it is meant that monitoring and dispensing components are integrated in an intelligent feedback system that is so small that it can be carried on the body of the patient without obstructing his movement, while it is continuously connected to the

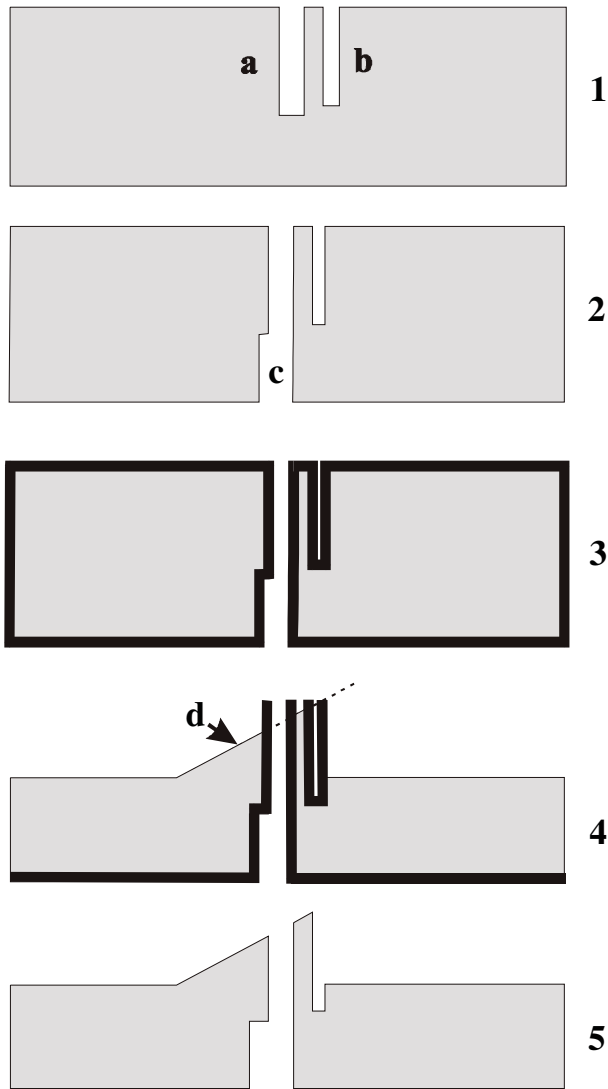
blood stream and releases the required drug whenever a certain monitor analyte reaches a critical value.

In this paper we focus on an essential part of the mentioned medical microsystems, viz. an array of micromachined hollow microneedles for transdermal liquid transfer. Such hollow needles can be used either for blood extraction, drug delivery, or both. Several approaches to the micromachining of this type of device are known, and roughly these can be divided in in-plane and out-of-plane designs. The in-plane version is the most convenient to fabricate with state-of-the-art planar technology [2-4], comprising surface micromachining and different techniques of silicon etching, and creates a good degree of flexibility with respect to needle design. However, the needle density that can be obtained is limited, while a high density is desirable in order to achieve acceptable liquid flow rates.

Well-known published examples of out-of-plane micromachined microneedles for transdermal applications [5,6] have as a disadvantage that their flat hollow tips tend to punch and therewith damage the skin, whilst the punched material may at least partially obstruct liquid flow through the needle. Promising results were obtained by Stoeber and Liepmann [7], who used directional Reactive Ion Etching (RIE) to define a narrow flow channel through a silicon wafer and thin film protection of this channel followed by isotropic etching from the other side of the wafer to fabricate the needle. This method allowed the fabrication of mechanically stable needles with a flow channel off-center of the needle tip, which reduces the punching problem described above. The radius of the tips was however relatively large and still needs further improvement.

## FABRICATION PROCESS

Fig.1 describes the fabrication process for an improved out-of-plane needle design. The method builds on the previously mentioned work of Stoeber et al. [7].

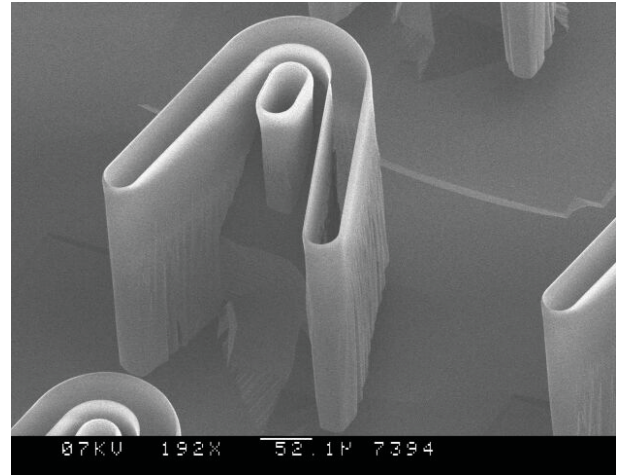


*Fig.1. Microneedle fabrication sequence. For an explanation of the symbols, see text. The figures have been stretched in horizontal direction for clarity.*

Essential features of the design are that the location of the opening does not coincide with the needle tip and can be positioned freely, a flow channel extending to the opposite side of the substrate leaving enough space for any desired fluidic component on that side, a high needle density, and a needle structure with excellent cutting properties.

The fabrication process starts with several cryogenic RIE steps: in a silicon {100} substrate a hole, **a** in Fig.1, with a cross-section corresponding to the desired flow properties of the needle, and a slot **b** which defines the position of the needle tip and the shape of the sidewalls of the needle, are etched simultaneously. It is essential that the slot is properly

positioned with respect to the crystallographic orientation of the substrate. A connecting hole **c** is etched by RIE from the back side of the wafer. In this step, it is also possible to include a fluidic channel structure on the backside of the substrate. Subsequently the inner surfaces of the holes and the slot are coated with a conformal layer that is resistant against KOH (in our case LPCVD silicon nitride).



*Fig.2. Slot and hole still coated with protective layer, after etching in KOH, needle height 400  $\mu\text{m}$ , base 250  $\mu\text{m}$ , hole diameter 70  $\mu\text{m}$*

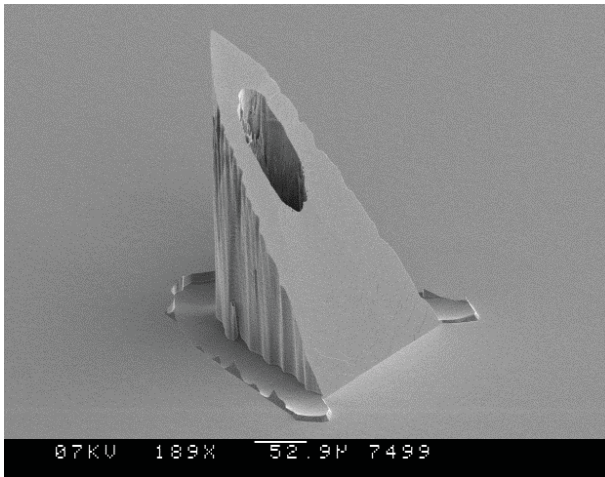
After removal of the protective layer at the top surface of the wafer, in step **4** anisotropic wet etching in a concentrated KOH solution is performed, which leaves a structure bound by a slow-etching {111} plane on one side, indicated by **d** in Fig.1. A similar method was used by Albrecht et al. to fabricate AFM tips [8]. The coated slot sidewalls prevent etching from other sides. Finally, the protective layer is stripped.

Fig. 2 shows the result after step **4**. In this particular case the needle was designed such that the tip had a defined curvature. The latter is determined by the design of the slot and its position with respect to the crystallographic orientation of the silicon substrate.

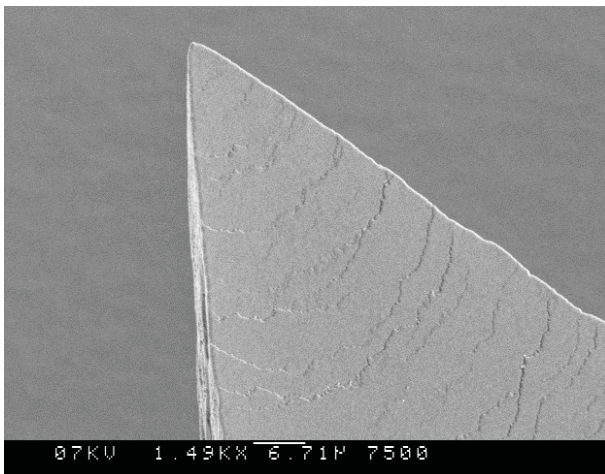
The advantage of this method over that of Stoeber et al., who etched the connecting hole from the backside up to the surface at which the needle tip is defined later, is that the essential lithographic definition of respective hole and needle tip positions in our case is done on the same side of the wafer, so that back-to-front alignment becomes less critical, and the shape of the flow channel at the position where it really matters, i.e. at the needle surface, is precisely defined.

## FABRICATION RESULTS

Fig.3 shows a typical result of a 400  $\mu\text{m}$  high microneedle with a triangular tip shape, a base of 250  $\mu\text{m}$ , and a maximum hole width of 70  $\mu\text{m}$ . The center of the in this case elliptical hole in the needle is positioned ca. 40  $\mu\text{m}$  from the tip of the needle. It can be seen that the vertical sidewall of the needle has a rough surface, which is a feature of the applied RIE process.



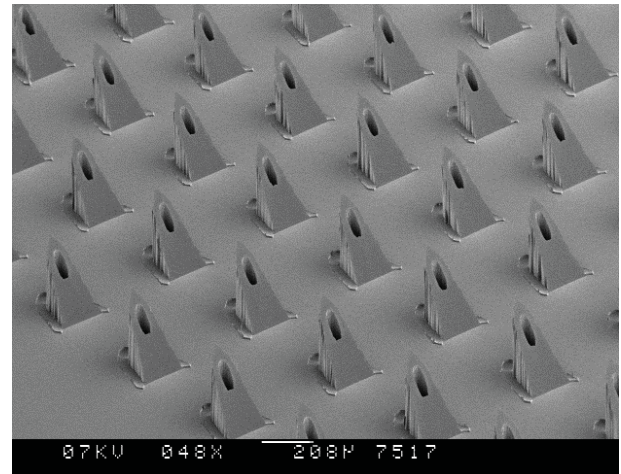
*Fig.3. SEM picture of 400  $\mu\text{m}$  high microneedle*



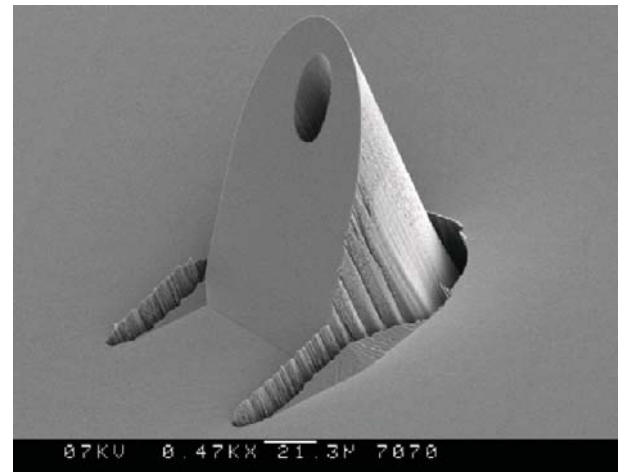
*Fig.4. Close-up of needle tip surface*

Fig.4 shows a close-up of the sloped sidewall of the needle, which is an almost perfect Si {111} surface. The picture shows a number of rather low steps, originating from the tip of the needle, where it originally was bound by the protective layer of the slot (see Fig.2). These steps are a typical feature of the chemical etching process on an atomically flat crystal plane that is in contact with a non-etching material [9]. The main implication of the steps is that

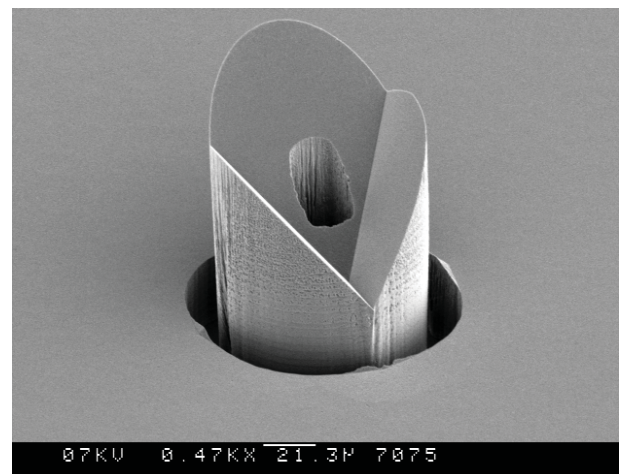
the angle between the needle surface and the surface of the substrate becomes slightly (1 or 2°) lower [9].



*Fig.5. Needle array with 555  $\mu\text{m}$  pitch*



*Fig.6. SEM picture of blade-type needle.*



*Fig.7. Gouge-shaped silicon needle.*



The presented fabrication method allows high needle densities, see Fig.5, with excellent uniformity across the wafer surface. Other needle tip designs can be achieved by changing the design of the slot. Two examples of the many possibilities are shown: Fig. 6 shows a design with a curved shape, while Fig. 7 shows a hollow chisel.

### PERFORMANCE TESTS

The performance of the needles was tested. A first test on a potato demonstrated that juices from the vegetable are drawn into the needle by capillary forces. This is an important feature of the device offering great potential for future applications, since liquid withdrawal can be achieved without external pumping means. Similar results were obtained from a test on human skin. Blood was easily withdrawn from the body, and puncture of the skin was found to be painless and without any remaining damage (Fig.8). None of the needles failed during puncture or withdrawal.

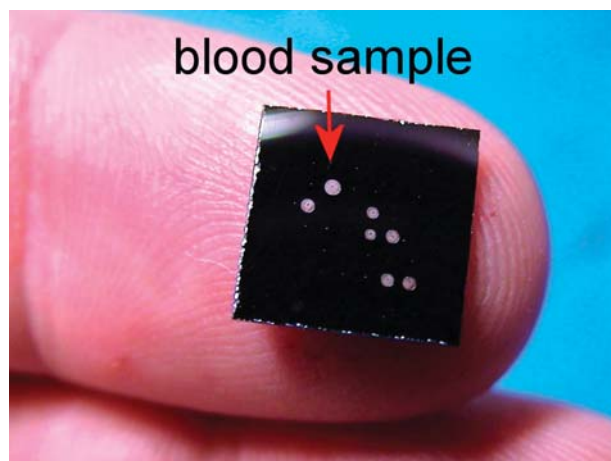


Fig.8. Blood sampling, using an array of needles. (white spots are droplets of blood)

### CONCLUSIONS

An improved design and versatile reproducible fabrication process for hollow micro needles [1] with proper mechanical strength and sharpness to be applied for painless transdermal transfer of blood were presented. Tests have shown that capillary forces draw the blood into the needle, reducing the need for external pumping means. Future research will focus on the connection of a complete micro system for blood analysis to the needle chip.

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